Citation:

Wright CB, Elkind MS, Luo X, Paik MC, Sacco RL. Reported alcohol consumption and cognitive decline: the northern Manhattan study. *Neuroepidemiology*. 2006; 27: 201-207.

PubMed ID: 17047373

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

- Measure the effect of alcohol intake on cognitive performance over time in a younger, multi-ethnic, community-based sample
- Assess the effect of having an apolipoprotein E ε4 (APOE-4) allele.

Inclusion Criteria:

- Resident of Northern Manhattan for three or more months
- English- or Spanish-speaking
- Resident of a household with a telephone
- Age 40 or more years
- No stroke diagnosis at enrollment or before the first cognitive assessment in 2001
- No history of alcohol-related hospitalization
- Data on reported alcohol intake
- Two or more cognitive function scores available
- Subjects provided written informed consent; the Columbia University Medical Center ethics committee approved the study.

Exclusion Criteria:

- Non-resident of Northern Manhattan, or resident for less than three months
- Not English- or Spanish-speaking
- Resident of a household without a telephone
- Age less than 40 years
- Stroke diagnosis either before enrollment or prior to the first cognitive assessment in 2001
- History of alcohol-related hospitalization
- No data on reported alcohol intake
- Less than two cognitive function scores available.

Description of Study Protocol:

Recruitment

Dual-frame, random digit dialing sample of subjects residing in Northern Manhattan.

Design

- Prospective cohort study with annual follow-ups
- At enrollment (sometime between 1993 and 2001), participants completed a telephone interview, physical examination and medical records review
- Participants completed subsequent annual telephone interviews
- Cognitive assessments were included beginning in 2001.

Dietary Intake/Dietary Assessment Methodology

Alcohol intake was measured in a structured interview adapted from food-frequency questionnaires (FFQ). It included responses for beer, wine and liquor, with nine frequency responses (none to seven or more drinks per day). At enrollment, subjects were asked about average consumption in the past year and average lifetime consumption. At the time of the cognitive assessment, subjects were asked about average consumption in the past six months.

Statistical Analysis

- Subjects who had a stroke sometime after the first cognitive assessment had all subsequent cognitive scores censored
- Generalized estimating equations were used to measure an association between reported alcohol intake at the first cognitive assessment and changes in cognitive scores over time, controlling for potential confounders, such as time between cognitive assessments, age, education, gender, race or ethnicity, health insurance status,high-density lipoprotein (HDL-C) level, body mass index (BMI), history of hypertension, diabetes, cardiac disease, current smoking, depression and physical inactivity
- Stratified analyses were repeated in a subset of the sample for whom APOE-4 allele status was known
- Potential bias due to dropouts was assessed in a logistic regression model. Drop-out after the first cognitive assessment was predicted by the first assessment score, reported alcohol intake, the interaction between the two and relevant covariates.

Data Collection Summary:

Timing of Measurements

- Subjects were enrolled sometime between 1993 and 2001. At enrollment, subjects completed a telephone interview, physical examination including lab assessment and medical records review.
- A subset (N=600) had APOE-4 allele status determined
- Subjects completed annual telephone interviews after enrollment. Cognitive assessment was included beginning in 2001.

Dependent Variables

Annual cognitive functioning (based on the modified Telephone Interview for Cognitive Status

[TICS-m]):

- TICS-m assesses orientation, attention, immediate recall of a 10-word list, calculations, judgment, language, finger tapping, antonyms and delayed recall of the 10-word list
- Scored out of 51 points; normally distributed without a ceiling effect and good validity and reliability in multi-ethnic community samples.

Independent Variables

Alcohol consumption in the previous six months months (five categories: never, past, less than one drink per week, one drink per week to two drinks per day, more than two drinks per day):

- Those who reported alcohol intake at enrollment, but not at the time of the first cognitive assessment were considered past drinkers
- Those who reported no intake at either enrollment or the first cognitive assessment were considered never drinkers
- Those whose intake at follow-up differed by two categories from enrollment were excluded (N=10).

Control Variables

- APOE-4 allele status (baseline fasting blood sample; determined by H-haI digestion and PCR amplification of genomic DNA)
- Time between cognitive assessments
- Sociodemographics:
    - Age (years)
    - Education
    - Gender
    - Race/ethnicity (self-reported as Hispanic, black, white or other groups)
- Health insurance status
- HDL-C level (baseline fasting blood sample, determined with an automated spectrometer)
- BMI
- Current smoking
- Physical inactivity
- History of medical conditions:
    - Hypertension (systolic blood pressure (SBP) higher than 140mmHg or diastolic blood pressure (DBP) higher than 90mmHg on the mean of two measures, self-reported diagnosis or medical treatment for hypertension)
    - Diabetes (fasting blood glucose 127mg per dL or higher, self-reported diagnosis or insulin or oral hypoglycemic use)
    - Cardiac disease (history of coronary artery disease, atrial fibrillation, or myocardial infarction)
    - Depression (Hamilton Depression Rating Scale score higher than 10 or history of antidepressant use).

Description of Actual Data Sample:

- *Initial N:* 3,298 enrolled between 1993 and 2001 (68% response rate)
- *Attrition (final N):*
    - 1,428 analyzed (43% of initial N); 6,913 person-years of follow-up (mean 2.2 years; range 0.5 to 4.4 years); 600 had APOE-4 allele status tested

- Subjects were excluded or lost to follow-up for history of alcohol-related hospitalization (N=31), death (N=812), stroke (N=128), insufficient data on alcohol intake or fewer than two cognitive assessment scores (N=851). 48 subjects were not accounted for
- Compared to those who were excluded, the sample had more Hispanics and diabetics and fewer blacks. There was no difference in cognitive scores or in the interaction between cognitive scores and alcohol intake among those who dropped out after the first cognitive assessment

- *Age:* Mean age 71 years
- *Ethnicity:* 62% Hispanic, 19% black, 19% white
- *Other relevant demographics:*
  - 12% uninsured, 45% on Medicaid, 43% privately insured
  - 82% had hypertension, 25% were diabetic, 19% had cardiac disease, 3% had a history of depression
  - 13% were current smokers
  - 21% were never drinkers, 44% were past drinkers
  - Of those tested, 155 were APOE-4 allele carriers and 445 were non-carriers
- *Anthropometrics:* BMI: (kg/m^2)
  - 27% less than 25
  - 43% 25 to 30
  - 30% higher than 30
- *Location:* Northern Manhattan.

Summary of Results:

Key Findings

- Mean TICS-m scores declined an average of 0.4 points from the first to the last assessment
- Amount of current (but not past) alcohol intake was positively associated with TICS-m scores over time
  - The association was diminished when adjusted for sociodemographic variables, but was still significant
  - Including vascular risk factors (Model three) further diminished the association, but more than one drink per week was still associated with higher cognitive function scores
- Neither baseline TICS-m scores nor changes over time differed significantly by APOE-4 allele status. Allele status did not modify the effect of intake on cognitive function.

	Never N=300	Past Drinkers		One Drink Per Month To Less Than One Per Week		One Drink Per Week To Two Per Day		More Than Two Drinks Per Day	
		N=622		N=145		N=330		N=31	
		β (95% CI)	P-value	β (95% CI)	P-value	β (95% CI)	P-value	β (95% CI)	P-value
Model one	Ref	0.6 (-0.2, 1.3)	0.14	1.5 (0.5, 2.5)	0.003	2.2 (1.3, 3.0)	<0.0001	2.9 (1.4, 4.4)	0.0002

Model two	Ref	0.3 (-0.4, 1.1)	0.40	1.0 (0.03, 1.9)	0.04	1.6 (0.7, 2.4)	0.0003	2.1 (0.6, 3.6)	0.008
Model three	Ref	0.4 (-0.4, 1.2)	0.36	0.9 (-1.2, 1.9)	0.09	1.5 (0.6, 2.4)	0.001	2.4 (0.8, 4.0)	0.003

Model one is adjusted for age and education; Model two is Model one plus gender, race/ethnicity and insurance status; Model three is Model two plus history of hypertension, diabetes, cardiac disease, physical inactivity, depression, current smoking, HDL-C level and BMI.

Other Findings

In a sensitivity analysis, those with a history of alcohol-related hospitalization (N=31) further attenuated the effect in the more than two drinks per day category, but was still significant.

Author Conclusion:

- Current drinkers had less cognitive decline than never drinkers, adjusting for sociodemographic and vascular risk factors. The findings are in general agreement with previous research
- The past drinking group did not differ from non-drinkers, which may partially be due to heterogeneity among past drinkers in terms of amount of past drinking and amount of time abstinent
- APOE-4 allele status did not alter the association.

Reviewer Comments:

- *Author-identified strengths:*
  - *Prospective design*
  - *Community-based sample including Hispanics and blacks (groups with higher risk of dementia)*
- *Author-identified limitations:*
  - *Current drinkers may be healthier than non-drinkers or past drinkers because the latter may be abstaining because of health problems. This potential bias was addressed by studying change scores*
  - *Non-drinkers tended to have lower sociodemographic characteristics than drinkers, which may have biased the findings toward the null*
  - *Cognitive function was assessed over the phone, which may not be as valid as a full neuropsychiatric exam*
- *Additional concerns with the article:*
  - *48 subjects were not accounted for from the initial 3,298 at enrollment to final analysis sample of 1,428*
  - *There was no description of how a sub-sample was selected for APOE-4 allele status determination*
  - *Table one stated that the mean age was 71; the text said mean age was 66 (range 40 to 98)*
  - *The initial response rate was 68%, and only 43% of initial cases were analyzed.*

Comparisons to population demographics were not discussed, so it is difficult to determine how representative the final sample was

- *Although alcohol type was included in the intake measure, any potential differences among beer, wine and liquor were not explored.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A

3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	???
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	No
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	No
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes

6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	N/A
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A

8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes